IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appellants: Oliver Peoples, Lara L. Madison and Galt W. Huisman

Serial No.: 09/364,847 Art Unit: 1652

Filed: July 30, 1999 Examiner: D. Steadman

For: *ENZYMES FOR BIOPOLYMER PRODUCTION*

Mail Stop Appeal Brief-Patents
Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

REPLY BRIEF

Sir:

This is a Brief in reply to the Examiner's Answer mailed October 2, 2003. A Request for Oral Hearing accompanies this Reply along with the appropriate fee of $145.00. It is believed the no additional fee is required with this submission. However, should an additional fee be required, the Commissioner is hereby authorized to charge the fee to Deposit Account No. 50-1868.

(6) ISSUES ON APPEAL

The issues presented on appeal are:

(1) whether claims 1-6 are adequately described as required by 35 U.S.C. 112, first paragraph;

(2) whether claims 1-3, 5, and 6 are obvious under 35 U.S.C. 103(a) over U.S. Patent No. 5,245,023 ("Peoples") in view of Trends Biotech. 9:226-231 ("Bulow"); and

(3) whether claim 4 is obvious under 35 U.S.C. 103(a) over Peoples, in view of Bulow as applied to claims 1-3, 5, and 6 and further in view of Argos (*J. Mol. Biol.* 211:943-958).

(8) ARGUMENTS

(b) Rejection under 35 U.S.C. § 112, first paragraph (written description)

Appellants affirm all of the arguments made in the Appeal Brief.

The appellants respectfully submit that appropriate examples of the claimed enzymes are known and publicly available. The appellants have actually reduced to practice representative examples. Nothing further is required. The appellants submit that for each of the claimed classes of enzymes, the amino acid sequence and a cDNA encoding the enzymes are known from multiple sources. Appellants provide evidence that not only is the function generally the same between enzymes of the same class, and between different sources, but that the degree of homology is such that the known and available genes can be used to isolate additional genes from other sources encoding the enzymes. Such information and technology was readily available and known at the time of filing the present application. The appellants again submit that the terms "phasins", "thiolase", "reductase", "beta-hydroxyacyl-ACP::coenzyme-A transferase", and "enoyl-CoA hydratase" readily convey distinguishing information concerning identity, via structure and function. One of ordinary skill in the art could easily visualize the identity of each termed protein. It is well established in the art that structure-function relationships do exist, and it is no more prevalent than within families of proteins, such as those that drive the specific reactions of claim 1.

(c) Rejections under 35 U.S.C. § 103

Appellants affirm all of the arguments made in the Appeal Brief.

U.S. Patent 5,245,023 to Peoples ("Peoples")

The claims are directed to fusion proteins expressed as catalytically active enzymes which act on substrate in successive reactions in a polyhydroxyalkanoate biosynthetic pathway. Peoples' suggestion that one may fuse the cloned and characterized polymerase genes (PHA and PHB) together, would not make obvious to one of ordinary skill in the art the presently claimed protein fusions. The phrase "[H]owever, the cloned and characterized genes can be further modified by constructing fusions of the two polymerases or by chemical mutagenesis" (see column 23, lines 16-19; here is the single mention of the term "fusion" in Peoples) would not lead one to the realization that **successive** enzymatic reactions could catalyzed *via* the heretofore unknown claimed protein fusions. It is clear that Peoples intended to create a ***single*** enzymatic polymerase structure from the suggested fusion (see, for example, column 23, lines 22-24). Altering an enzyme's specificity suggests there is a modification of ***a single*** enzyme's substrate binding pocket, such that alternative substrates may be recognized and incorporated into ***one*** polymer (see, for example, column 23, lines 22-24; "[T]his is a *straightforward approach* to ***altering the enzyme's specificity to create novel polymerases***" emphasis added). This is in complete contrast to the presently claimed protein fusions, wherein two or more ***separate enzymes*** are fused together and *each enzyme's product serves as a substrate for the "next"*

enzyme to which it is fused. Again, one of ordinary skill in the art would not find the present claims obvious in view of Peoples.

Trends in Biotech by Bulow ("Bulow")

Bulow suggests optimal length linkers for the enzymes described therein. The choice of linkers is based upon the correct folding and accessibility of active sites in each of the enzymes. Bulow's statements relating to enzyme technology and its usefulness in the development of metabolic engineering are entirely prophetic. Such suggestions do not create an expectation of success without evidence suggesting the modification (i.e. fusion catalyzing successive reactions) would be successful.

Summary

The combination of Peoples and Bulow does not render obvious the presently claimed protein fusions. There is nothing to suggest that a reasonable expectation of success could be based upon the two cited references. Peoples uses recombinant technology to alter the enzyme binding characteristics ***of a single enzyme***. Appellants respectfully submit that such a reference, solely in combination with Bulow, cannot be properly used to deny allowance of the claims on appeal. The foregoing discussion under 35 U.S.C. § 103 applies to claims 1-3, 5, and 6; *and claim 4.*

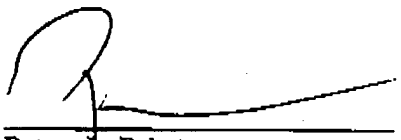
(d) Individual Examination of Dependent Claims

Groups 2 and 4 of the claims must be considered separately because of the essential elements unique to each group. For example, claims 5 and 6 are directed to fusion proteins being

expressed in host cells. Claim 2 is directed to fusion proteins harboring catalytically active enzymes. The issues with regard to obviousness and written description for each group are different. No art has been cited to show that the fusions of claims 5 and 6, in a host bacterium or plant, would be obvious to one of ordinary skill in the art. No art has been cited to explicitly show that the enzymes of claim 2 (catalytically active in a fusion protein) would be rendered obvious.

For the foregoing reasons and those in the Appeal Brief, Appellants submit that claims 1-6 are patentable.

Respectfully submitted,



Patrea L. Pabst
Reg. No. 31,284

Date: December 2, 2003

HOLLAND & KNIGHT LLP
One Atlantic Center, Suite 2000
1201 West Peachtree Street
Atlanta, Georgia 30309-3400
(404) 817-8473
(404) 817-8588 (fax)

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I hereby certify that this paper, along with any paper referred to as being attached or enclosed, is being deposited with the United States Postal Service on the date shown below with sufficient postage as first-class mail in an envelope addressed to the Mail Stop Appeal Brief-Patents, Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313.

Peggy Bailey

Date: December 2, 2003

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